

Peer Review File

Article Information: <https://dx.doi.org/10.21037/gc-23-520>

Reviewer A

This is an interesting commentary on an important contribution to the literature.

Comment 1: The authors should make comment on the method used for volumetric measurements (ie limb circumferential measurements) and the strengths and shortcomings of the technique used.

Reply 1: This is discussed in lines 60-70 in the original manuscript and we have added more information as below. The strengths are discussed on page 3, lines 82-83.

Changes in the text: We added a description of the method (see page 3, lines 79-81), as well as a line on a challenge with the method (see page 3, lines 85-86).

Comment 2: * The authors should also make mention that statistical significance can change between an interim and final analysis depending on a few additional patients developing lymphedema in the intervention arm, and therefore these preliminary results are not reliable until the trial is fully reported.

Reply 2: Than you, this has been added as below.

Changes in the text: Please see page 2, lines 70-71.

Comment 3: Please can the authors explain the intention for '(is it available?)' on line 97, the meaning is unclear.

Reply 3: Very sorry, this was an error left in the text.

Changes in the text: This has been deleted from line 114.

Reviewer B

This is a well written editorial putting this important and well-designed study by Corridi et al in the context of previous work in this area. I have a couple points that the authors might want to consider discussing:

Comment 1: The patients were not blinded in this study and this could impact a patient's adherence to therapy as well as the patient's perception and reporting of outcomes. While it was postulated that the control patients might be more motivated to comply with lymphatic compression and that this might provide further support that the benefits of the intervention were significant, it might also make these patients more anxious about any symptoms they experience and more likely to report negative symptoms, which would lessen the reported benefits seen using PROMs.

Reply 1: This is a very good point!

Changes in the text: This point has been added to page 3, lines 111-113.

Comment 2: Given that many patients were radiated, it will be important to follow patients for several years to ascertain if late fibrosis leads to occlusion of some lymphovenous anastomoses, mitigating some of the early benefits that have been reported.

Reply 2: Another very good point that we have addressed.

Changes in the text: Please see page 4, lines 139-141.

Reviewer C

Comment 1: A thorough and well-written editorial on the efficacy of immediate lymphatic reconstruction for preventing the development of lymphedema.

Reply 1: Thank you very much.

Changes in the text: None

Reviewer D

Comment 1: Breast cancer related lymphedema (BCRL) occurs in 25% to 35% of patients after axillary lymph node dissection (ALND), leading to lifelong functional and social challenges. One of preventative approaches is immediate lymphatic reconstruction (ILR), using lymphovenous anastomosis completed at the time of ALND. Recently, Coriddi et al. have published preliminary results of randomized control trial (RCT). This trial is the first of its kind to randomize breast cancer patients undergoing ALND to either ILR (ILR group) or standard care, ALND only (control group). Consequently, they found the cumulative incidence of BCRL to be significantly lower in the ILR group than in the control group (9.5% vs. 32%; $p=0.014$). I agree with Yakaback's review that the preliminary results of the RCT by Coriddi et al. show promise for the efficacy of ILR and represent an essential step in moving this procedure forward. However, patients undergoing ALND do not always develop BCRL. Moreover, ILR is a microscopic surgery and takes between 30 and 60 minutes to complete. Therefore, it is required to predict the patients who develop BCRL after ALND. As Coriddi et al. reported, bioimpedance is not as accurate as ICG lymphography in detecting lymphatic flow disruption. It is interesting whether ICG fluorescent lymphography is useful to detect lymphatic flow disruption just after ALND. Further studies are needed.

Reply 1: This is a very strong point as it would be very useful to predict who goes on to develop lymphedema and therefore be able not do the procedure on low-risk patients, which reduces risk and saves time and money.

Changes in the text: This has been added into the text. Please see page 4, lines 145-148.

Reviewer E

Comment 1: I haven't read the paper that the editorial reviews but the questions/notes I made in the beginning paragraphs were discussed and questioned further on. I think it is a well-

balanced piece that supports the want for better treatment/prevention of lymphoedema and acknowledges the current limitations in practice.

Reply 1: Thank you very much.

Changes in the text: None

Reviewer F

Comment 1: Please further discuss the practice of immediate lymphatic reconstruction (ILR), using lymphovenous anastomosis (LVA) in term of its cost effectiveness

Comment 1: A good point that we should have included. There has been a prior publication that has shown that it is cost effective.

Changes in the text. This has been added into the text as well as into the bibliography. Please see page 2, lines 51-52.